

**Claims**

- 1 A method for the diagnosis of a polymorphism in P2X<sub>7</sub> in a human, which method comprises determining the sequence of the human at one or more of the following positions: positions 936, 1012, 1147, 1343 and 1476 in the 5'UTR region of the P2X<sub>7</sub> gene as defined by 5 the position in SEQ ID NO: 1;
- positions 253, 488, 489, 760, 835, 853, 1068, 1096, 1315, 1324, 1405, 1448, 1494, 1513, 1628 and 1772 in the coding region of the P2X<sub>7</sub> gene as defined by the position in SEQ ID NO: 2; and
- positions 4780, 4845, 4849, 5021, 5554, 5579, 5535, 5845 and 6911 in the intron region of 10 the P2X<sub>7</sub> gene as defined by the position in SEQ ID NO: 3;
- positions 76, 155, 245, 270, 276, 348, 357, 430, 433, 460, 490 and 496 in the P2X<sub>7</sub> polypeptide as defined by the position in SEQ ID NO: 4;
- and determining the status of the human by reference to polymorphism in P2X<sub>7</sub>.
- 2 Use of a diagnostic method as defined in claim 1 to assess the pharmacogenetics of a 15 drug acting at P2X<sub>7</sub>.
- 3 A polynucleotide comprising at least 20 bases of the human P2X<sub>7</sub> gene and comprising an allelic variant selected from any one of the following:

Region	Variant SEQ ID NO: 1
5'UTR	936 A
	1012 C
	1147 G
	1343 A
	1476 G

Region	Variant SEQ ID NO: 2
exon 2	253 C
exon 5	488 A
	489 T
exon 7	760 G
exon 8	835 A
	853 A
exon 11	1068 A
	1096 G
exon 12	1315 G
exon 13	1324 T
	1405 G

	1448 T
	1494 G
	1513 C
	1628 T
	1772 A

Region	Variant SEQ ID NO: 3
intron E	4780 T 4845 T 4849 C
intron F	5021 C 5554 (GTTT) <sub>n</sub> , n=4 5579 C 5535 T
intron G	5845 T 6911 C

- 4 A nucleotide primer which can detect a polymorphism as defined in claim 1.
- 5 An allele specific primer capable of detecting a P2X<sub>7</sub> gene polymorphism as defined in claim 1.
- 5 6 An allele-specific oligonucleotide probe capable of detecting a P2X<sub>7</sub> gene polymorphism as defined in claim 1.
- 7 Use of a P2X<sub>7</sub> gene polymorphism as defined in claim 1 as a genetic marker in a linkage study.
- 8 A method of treating a human in need of treatment with a drug acting at P2X<sub>7</sub> in
- 10 which the method comprises:
- i) diagnosis of a polymorphism in P2X<sub>7</sub> in the human, which diagnosis preferably comprises determining the sequence at one or more of the following positions: positions 936, 1012, 1147, 1343 and 1476 in the 5'UTR region of the P2X<sub>7</sub> gene as defined by the position in SEQ ID NO: 1;
- 15 positions 253, 488, 489, 760, 835, 853, 1068, 1096, 1315, 1324, 1405, 1448, 1494, 1513, 1628 and 1772 in the coding region of the P2X<sub>7</sub> gene as defined by the position in SEQ ID NO: 2; and
- positions 4780, 4845, 4849, 5021, 5554, 5579, 5535, 5845 and 6911 in the intron region of the P2X<sub>7</sub> gene as defined by the position in SEQ ID NO: 3; and
- 20 positions 76, 155, 245, 270, 276, 348, 357, 430, 433, 460, 490 and 496 in the P2X<sub>7</sub> polypeptide as defined by the position in SEQ ID NO: 4;

and determining the status of the human by reference to polymorphism in P2X<sub>7</sub>; and

ii) administering an effective amount of the drug.

9 An allelic variant of human P2X<sub>7</sub> polypeptide comprising at least one of the following:

a alanine at position 76 of SEQ ID NO 4;

5 a tyrosine at position 155 of SEQ ID NO 4;

a glycine at position 245 of SEQ ID NO 4;

a histidine at position 270 of SEQ ID NO 4;

a histidine at position 276 of SEQ ID NO 4;

a threonine at position 348 of SEQ ID NO 4;

10 a serine at position 357 of SEQ ID NO 4;

a arginine at position 430 of SEQ ID NO 4;

a valine at position 433 of SEQ ID NO 4;

a arginine at position 460 of SEQ ID NO 4;

a glycine at position 490 of SEQ ID NO 4; and

15 a glutamic acid at position 496 of SEQ ID NO 4;

or a fragment thereof comprising at least 10 amino acids provided that the fragment comprises at least one allelic variant.

10 An antibody specific for an allelic variant of human P2X<sub>7</sub> polypeptide as defined in claim 9.

20 11. A polynucleotide comprising any one of the following twenty six P2X<sub>7</sub> haplotypes:

	<b>1012</b>	<b>489</b>	<b>5579</b>	<b>835</b>	<b>853</b>	<b>1068</b>	<b>1096</b>	<b>1405</b>	<b>1513</b>
	SEQ ID	SEQ ID	SEQ	SEQ	SEQ	SEQ	SEQ	SEQ	SEQ ID
	1	2	ID 3	ID 2	ID 2	ID 2	ID 2	ID 2	2
<b>1</b>	T	T	C	G	G	A	G	A	A
<b>2</b>	C	C	G	G	G	C	A	A	A
<b>3</b>	C	C	C	A	G	C	A	C	
<b>4</b>	C	T	G	G	A	C	G	A	
<b>5</b>	C	C	G	G	A	G	A	A	
<b>6</b>	C	C	C	A	G	C	A	A	
<b>7</b>	T	T	G	G	A	C	G	A	
<b>8</b>	C	T	C	G	G	C	A	A	
<b>9</b>	C	C	C	G	G	C	A	A	
<b>10</b>	C	T	G	G	G	C	A	C	
<b>11</b>	T	C	G	G	A	C	A	A	
<b>12</b>	C	T	C	G	G	C	A	C	

13	T	C	C	G	G	A	C	A	A
14	T	C	C	G	G	G	C	A	C
15	C	T	C	G	G	A	C	A	A
16	T	T	C	G	G	A	C	G	A
17	C	C	G	G	G	A	C	G	A
18	T	C	G	A	A	G	C	A	A
19	C	C	C	G	G	G	G	A	A
20	T	C	C	G	G	G	G	A	A
21	C	T	C	A	G	G	C	A	A
22	C	C	C	G	G	G	C	A	C
23	C	T	G	G	A	A	G	G	A
24	T	T	G	G	G	A	G	G	A
25	C	T	C	G	G	G	G	A	A
26	C	C	C	G	G	G	C	A	A

12 A human P2X<sub>7</sub> polypeptide comprising one of the following eighteen combinations of allelic variant determined amino acids based on positions identified in SEQ ID NO: 4:

	155	270	276	348	357	460	496
1	Y	R	R	T	S	Q	E
2	Y	R	R	T	T	R	E
3	Y	R	R	T	T	Q	E
4	Y	R	R	T	S	R	E
5	Y	R	R	A	T	Q	A
6	Y	R	R	A	T	Q	E
7	Y	R	R	A	S	Q	E
8	Y	R	H	T	S	R	E
9	Y	H	R	A	T	Q	E
10	H	R	R	T	T	Q	E
11	H	R	R	T	T	R	E
12	H	R	R	A	T	Q	A
13	H	R	R	A	S	Q	E
14	H	R	R	A	T	Q	E
15	H	R	R	T	S	Q	E
16	H	H	R	A	T	Q	A
17	H	H	R	A	T	Q	E
18	H	H	H	A	T	Q	E

13 A polynucleotide which encodes any human P2X<sub>7</sub> polypeptide as defined in claim 12.